PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Large Care Gaps in Primary Care Management of Asthma: A Longitudinal Practice Audit
AUTHORS	Price, Courtney; Agarwal, Gina; Chan, David; Goel, Sanjeev; Kaplan, Alan; Boulet, Louis-Philippe; Mamdani, Muhammad; Straus, Sharon; Lebovic, Gerald; Gupta, Samir

VERSION 1 – REVIEW

REVIEWER	Dr Duncan Keeley General Practitioner Thame Oxfordshire UK
REVIEW RETURNED	20-Mar-2018

GENERAL COMMENTS	This is an important and original cohort study of asthma patients in there primary care practices in Canada using electronic record review to document key features of asthma care process over one year (2012-2013) 45% of physicians in participating practices agreed to take part and stat on 884 patients reported. Inclusion and exclusion criteria are sensible and well described. Patients with active (billed-for or receiving COPD - specific medication) were excluded , but 10% of patients had a recorded co-moribdity of COPD (see Table) This point perhaps requires explicit clarification in the text of the article. Methods of data extraction are clearly described and the inter-observer variation in record assessment is reported. Very low rates of documented adherence to key aspects of recommended asthma care process was found. Statistical analysis appears sound to this non-statistician. The discussion is balanced and sensible and contains an appropriate assessment of study limitations. Some more detailed suggestions as to how the poor level of documented adherence to key guideline recommendations could be improved might be worthwhile. References are comprehensive and relevant.

REVIEWER	Levon Utidjian Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA
REVIEW RETURNED	30-Mar-2018

| **GENERAL COMMENTS** | Thank you for submitting this article on provider adherence to adult asthma practices in a primary care setting. It is an important topic and the perspective examining provider adherence through electronic audit to identify patients shows another reason why EHR data is so useful in cohort creation.

The following edits and clarifications will help the reader better understand your article.

Abstract:
-The results section could be clearer by indicating which are primary and secondary outcomes. The two sentences that start 'Assessment occurred more often …' are confusing and could benefit from different wording to distinguish them. The second sentence is also very long and could be broken up to improving reading.

Article Summary:
-Regarding bullet 2, what made this multivariable modelling so novel? Had this particular set of covariates not been modeled before?
-Bullet 5 is awkward sounding with 'included sites included…'; perhaps change to 'study sites included…'

Background:
-The background is very thorough and well referenced, but could read better with the second paragraph being broken up into smaller paragraphs.

Methods:
-Study design should mention the diagnostic billing codes are ICD9 codes.
-Was this prospective cohort study exempt from IRB Review, or was review obtained but not mentioned?
-Data collection: The mention of an electronic audit in this article led me to believe that apart from patient identification, the paper would describe electronic methods to extract the provider performance of the outcomes of interest, like looking for changes in asthma medications for escalation/de-escalation, identification of specific control assessment questions and the presence of an AAP in the chart through processes like string matching or natural language processing. However, it appears that this information was obtained by manual chart review with entry into an Excel form. I would recommend considering changing the title of the article.
-Also in Data collection: line 27, you do not have to redefine the acronym ED again (previously done in Background).
-Outcomes: line 10, you do not have to redefine the acronym ED again.

Results:
-How was most responsible physician (MRP) determined? Was each patient only ever associated with one physician? Were eligible visits only those with the MRP or could they be with other providers?
-Asthma Care: The sub-sections could be improved by reiterating which measures were primary and secondary objectives, and presenting them in that order.

Discussion:
-page 11, line 22, there are 2 periods at the end of the sentence.
-page 13, line 33, remove the 'of' in 'several of limitations'
-In the limitations section, was there any concern that the different |

	sites, although on the same EMR, could have had different reminders or other forms of decisions support that could have influenced provider performance?

REVIEWER	Eduardo Calvo Corbella Facultad de Medicina UAM Madrid. Spain.
REVIEW RETURNED	07-May-2018

GENERAL COMMENTS	It is an interesting work to fill gaps in the knowledge of primary care. They describe correctly the state of the question, but the objectives are not clearly stated. They state what they are going to do but they do not clearly define the objective until the "outcomes" section arrives. In the summary they say that it is "largest practice-based Audit" and should point out that this is the case in prospective studies, since other have analyzed part of the aspects related to "adherence in the practice of asthma management". About the design of the study, it is not clear who refused to participate and if this population (health servers)is very different from that of the participants. Regarding the concept of control, included in table 1, it does not follow the GINA or NICE criteria, but only the Canadian consensus (ref 8) although it cites it in the reference. Finally, The title does not accurately describe the content of the article

REVIEWER	Rita Amaral 1 - CINTESIS- Center for Health Technology and Services Research, Faculty of Medicine, University of Porto, Porto, Portugal 2 - Department of Cardiovascular and Respiratory Sciences, Porto Health School, Porto, Portugal
REVIEW RETURNED	25-Jun-2018

GENERAL COMMENTS	This is an interesting article that aims to measure adherence to key evidence-based adult asthma practices in primary care and to identify predictors of these behaviors, in a large practice-based audit of primary care. However, there are some methodologic issues that should be improved. - ABSTRACT Results: A 95% confidence interval for both proportions should be mentioned. Also, p-values should be addressed when the factors that significantly influenced the outcome are mentioned. - ARTICLE SUMMARY Use of term "novel" in multivariable modeling appears odd, considering that authors used multivariable logistic regression, one of the most widely known modeling techniques. - MANUSCRIPT 1. The introduction is well written but 2nd paragraph needs to be a bit shorter. Perhaps, divide into 2 smaller paragraphs. My concern is that this paragraph is a bit too long and the authors will lose the reader. 2. STROBE reporting guidelines appear to have been followed by the authors, however, it is not mentioned/cited in the manuscript. 3. It is not clear if there was a previous ethical approval of the study. Please clarify it.

4. Outcomes: The a priori choice of the co-variates as "clinically-relevant" must be supported by the literature.
5. Analysis: Please indicate what specifically the interrater reliability measures. I believe that the percent agreement (the concept of "agreement among raters") is fairly simple. Did the authors consider a more complex method (such as kappa statistic) to measure interrater reliability? Please comment the use of percent agreement considering its inability to account for chance agreement.
6. Multivariable logistic regression was used to identify predictors of each outcome. However, univariate analysis is also calculated but it is not mentioned in this section. Please cite it. Moreover, the odds ratio were also presented in the tables, but not mentioned in this section.
7. In order to interpret results of the multivariable analysis the assessment of the model goodness-of-fit is essential. However, this information is not in the manuscript. Also, it is not clear what variable selection procedure was used (FORWARD, BACKWARD, and STEPWISE). Please present this information and if statistic revealed good fitting in the final models.
8. The authors performed the multivariate logistic analysis in the 4199 eligible visits, however, it is unclear if they used only data from the first (baseline) visit. If not, a sensitivity analysis using only the data from the 1st visit should be considered and discussed to reduce bias.
9. Importantly, a subgroup analysis must be performed considering the different practice sites to address any clustering effect.
10. In pages 9 and 10, when authors mention "significant predictors", p-values must be cited. Also, the expression " was less/more likely" must be used citing a measure of probability such as odds ratio, rather than absolute or relative frequencies as the authors did. Please correct this.
11. Results presented in Table 3 and 4 must be improved. Presenting both columns ("Controller not initiated or escalated" and "Controller initiated or escalated") is redundant, and other information can be added, such as indicating the reference category for each variable used in the logistic model, and ultimately, presenting adjusted odds ratios and their respective 95% Confidence Intervals.
12. The study of the authors (Sá-Sousa et al. Rev Port Pneu 2014) reported that most patients with non-controlled asthma (88%) perceived their disease as controlled, I, which may hinder them from seeking better asthma control. Please discuss how patient's perception of the symptoms may have influenced the fact that physician did not assess asthma control?

REVIEWER	Soyiri IN
	United Kingdom
REVIEW RETURNED	05-Jul-2018

| GENERAL COMMENTS | I have reviewed the manuscript ID bmjopen-2018-022506 entitled "Large Care Gaps in Primary Care Management of Asthma: A Longitudinal Electronic Practice Audit" by Ms Price and colleagues. I reviewed the manuscript focusing on the choice of the statistical methods and analyses. I find the methods adequate. |
| | With regards to the tables and estimates, I have no comments for table 1. The summary measures and p-value estimates in tables 2, 3 and 4 are well presented. There aren't any obvious records/numbers that may suggest out of range errors. |

Reviewer 1

1. This is an important and original cohort study of asthma patients in there primary care practices in Canada using electronic record review to document key features of asthma care process over one year (2012-2013)

45% of physicians in participating practices agreed to take part and stat on 884 patients reported. Inclusion and exclusion criteria are sensible and well described. Patients with active (billed-for or receiving COPD - specific medication) were excluded, but 10% of patients had a recorded co-moribdity of COPD (see Table) This point perhaps requires explicit clarification in the text of the article.

RESPONSE: This is a fair point. As the reviewer notes, a validated EMR search-based algorithm was used to attempt to exclude patients with COPD based on billing codes or recent COPD-specific medication prescriptions. However, during the detailed chart review process, some patients with asthma were noted to have a COPD diagnosis documented either somewhere in the primary care chart or in a scanned specialist consultation note. These are the 7.7% of patients who had asthma-COPD overlap (Table 1). We have added this detail to the manuscript (page 10, paragraph 1).

2. Methods of data extraction are clearly described and the inter-observer variation in record assessment is reported. Very low rates of documented adherence to key aspects of recommended asthma care process was found.

Statistical analysis appears sound to this non-statistician.

The discussion is balanced and sensible and contains an appropriate assessment of study limitations. Some more detailed suggestions as to how the poor level of documented adherence to key guideline recommendations could be improved might be worthwhile.

References are comprehensive and relevant.

RESPONSE: We embedded suggestions for ways to address each gap in each relevant section in the discussion, based on prior literature, known barriers, and behavioural predictors identified in our study's models. We have now emphasized these suggestions and elaborated upon them (page 12, paragraph 1; page 13, paragraph 1; page 14, paragraph 1).

Reviewer 2

1. Abstract:

The results section could be clearer by indicating which are primary and secondary outcomes. The two sentences that start 'Assessment occurred more often …' are confusing and could benefit from different wording to distinguish them. The second sentence is also very long and could be broken up to improving reading.

RESPONSE: We have made the requested changes (Abstract; Page 3, Results section).

2. Article Summary:

-Regarding bullet 2, what made this multivariable modelling so novel? Had this particular set of covariates not been modeled before?

RESPONSE: To our knowledge, these covariates have not previously been modeled as predictors of asthma care performance. However, we agree that use of the phrase "novel multivariable modelling" might imply that the modeling method itself was novel, which was not the intention. Accordingly, we have removed the term "novel" from this phrase and instead replaced "…identification of behavioural predictors "with "identification of novel behavioural predictors" (Page 4, bullet 2).

-Bullet 5 is awkward sounding with 'included sites included…'; perhaps change to 'study sites included…'

RESPONSE: We have made the suggested change (Page 4, bullet 5).

3. Background:
-The background is very thorough and well referenced, but could read better with the second paragraph being broken up into smaller paragraphs.

RESPONSE: We agree with this reviewer's recommendation and have broken the second paragraph into 3 sub-paragraphs, each describing a different control criterion. We believe this improves readability (Pages 5 and 6).

4. Methods:
-Study design should mention the diagnostic billing codes are ICD9 codes.

RESPONSE: We have included this information (page 6, paragraph 3).

5. Was this prospective cohort study exempt from IRB Review, or was review obtained but not mentioned?

RESPONSE: Review was obtained at the principal investigator's hospital, and at the University overseeing the academic primary care sites. This information has been added (page 6, paragraph 3).

6. Data collection: The mention of an electronic audit in this article led me to believe that apart from patient identification, the paper would describe electronic methods to extract the provider performance of the outcomes of interest, like looking for changes in asthma medications for escalation/de-escalation, identification of specific control assessment questions and the presence of an AAP in the chart through processes like string matching or natural language processing. However, it appears that this information was obtained by manual chart review with entry into an Excel form. I would recommend considering changing the title of the article.

RESPONSE: Thank you for this feedback. We have removed the word "Electronic" from this title to avoid confusion regarding the manner in which we obtained information for this study (Page 1, Title).

6. Also in Data collection: line 27, you do not have to redefine the acronym ED again (previously done in Background).
RESPONSE: We have removed the duplicative information (page 7, paragraph 2).

7. Outcomes: line 10, you do not have to redefine the acronym ED again.

RESPONSE: We have removed the duplicative information (page 8, paragraph 3).

8. Results: -How was most responsible physician (MRP) determined? Was each patient only ever associated with one physician? Were eligible visits only those with the MRP or could they be with other providers?

RESPONSE: In Ontario, the most responsible physician (MRP) is determined by a registration process whereby the patient registers with a certain physician in the practice. This is the physician who is primarily responsible for their care. However, in certain circumstances, such as for urgent

matters, patients could be seen by another provider in the same practice who happened to be available. As a pragmatic study, we aimed to include all visits, including those that occurred with a non-MRP. However, we measured the impact of an MRP versus non-MRP visit on care behavior by including this as a covariate in our multivariable models. We have now clarified that patients could be seen by a clinician other than their MRP (page 9, paragraph 3).

9. -Asthma Care: The sub-sections could be improved by reiterating which measures were primary and secondary objectives, and presenting them in that order.

RESPONSE: We agree with this reviewer and this suggestion to clarify the primary/secondary measures was made by another reviewer for the abstract. We have added these sub-headings in the "Results" section under "Asthma Care" and moved the paragraph describing the poor control patient population below the primary outcome result (Pages 10 and 11).

10. Discussion:
-page 11, line 22, there are 2 periods at the end of the sentence.

RESPONSE: This has been removed (Page 12, paragraph 2).

11. page 13, line 33, remove the 'of' in 'several of limitations'

RESPONSE: This has been removed (Page 15, paragraph 1).

12. In the limitations section, was there any concern that the different sites, although on the same EMR, could have had different reminders or other forms of decisions support that could have influenced provider performance?

RESPONSE: We selected sites to represent the typical practice environment in our jurisdiction, which required no dedicated asthma resources on site, including no decision support tools for asthma. We have specified this in the text (Page 6, paragraph 3).

Reviewer 3
1.They describe correctly the state of the question, but the objectives are not clearly stated. They state what they are going to do but they do not clearly define the objective until the "outcomes" section arrives.

RESPONSE: We agree with this reviewer that the introduction could more clearly articulate the objectives of our study. We have re-phrased the last paragraph to explicitly state that our objective was to assess adherence to key asthma management practices and their predictors (Page 6, paragraph 1). As per another reviewer's recommendation, we have also divided the introduction into smaller sub-paragraphs, each addressing one of the 3 key care gaps that we aimed to study. Similarly, we have now explicitly labeled the primary and secondary outcomes both in the abstract and in the "Results" section to ensure that readers are clear about the study's focus and key findings.

2. In the summary they say that it is "largest practice-based Audit" and should point out that this is the case in prospective studies, since other have analyzed part of the aspects related to "adherence in the practice of asthma management".

RESPONSE: We have adjusted the first bullet to reflect that this is the largest "prospective practice-based audit…" (Page 4, bullet 1).

3. About the design of the study, it is not clear who refused to participate and if this population (health servers) is very different from that of the participants.

RESPONSE: Unfortunately, we were not able to collect data about clinicians who refused to participate, as they had not consented to the study. As in most studies of this type, participation bias must be considered. However, one might expect that those who volunteered for the study had an interest in asthma, and also that they might have improved their behavior once they knew they were being observed (Hawthorne Effect). Both factors would be bias towards smaller care gaps among included clinicians, which only reinforces our study finding of concerningly large care gaps. Even more importantly, given the unique practice environment in family health teams, whereby a given patient could be seen by clinicians other than their most responsible physician (MRP), our actual analytic sample ultimately reflected the asthma care behaviour of the entire practice (108 residents, 46 staff physicians, 17 nurse practitioners, and 2 physician assistants). This has been clarified (Page 9, paragraph 3).

4. Regarding the concept of control, included in table 1, it does not follow the GINA or NICE criteria, but only the Canadian consensus (ref 8) although it cites it in the reference.

RESPONSE: We had included GINA and NICE references for this table since criteria for "uncontrolled asthma" are similar in those guidelines to those in the Canadian guidelines. However, given that the exact criteria in the table are indeed reflective of the Canadian Asthma Guidelines, we have now removed the GINA and NICE references (Page 20, Table 1).

5. Finally, The title does not accurately describe the content of the article

RESPONSE: As recommended by another reviewer, we have changed the title of the article to remove the word "Electronic," thus better reflecting the manual practice audit methodology we used to measure asthma care gaps.

Reviewer 4
1. - ABSTRACT
Results: A 95% confidence interval for both proportions should be mentioned. Also, p-values should be addressed when the factors that significantly influenced the outcome are mentioned.

RESPONSE: We have added the p-values for all significant predictors (Page 3, Abstract). Unfortunately, since these results come from Chi-Square tests with more than two categories, it was not possible to report 95% confidence intervals on the difference of proportions.

2. ARTICLE SUMMARY
Use of term "novel" in multivariable modeling appears odd, considering that authors used multivariable logistic regression, one of the most widely known modeling techniques.

RESPONSE: Our intention was to indicate that the covariates we report have not previously been modeled as predictors of asthma care performance. However, we agree that use of the phrase "novel multivariable modelling" might imply that the modeling method itself was novel, which was not the intention. Accordingly, we have removed the term "novel" from this phrase (Page 4, bullet 2).

3. MANUSCRIPT
1. The introduction is well written but 2nd paragraph needs to be a bit shorter. Perhaps, divide into 2 smaller paragraphs. My concern is that this paragraph is a bit too long and the authors will lose the

reader.

RESPONSE: In accordance with this reviewer and another reviewer's recommendation, we have now divided the second paragraph into 3 sub-paragraphs, each describing a specific care gap (Pages 5 and 6).

2. STROBE reporting guidelines appear to have been followed by the authors, however, it is not mentioned/cited in the manuscript.
RESPONSE: We have now mentioned and cited STROBE in the methods (Page 6, paragraph 2).

3. It is not clear if there was a previous ethical approval of the study. Please clarify it.

RESPONSE: Review was obtained at the principal investigator's hospital, and at the University overseeing the academic primary care sites. This information has been added (page 6, paragraph 3).

4. Outcomes: The a priori choice of the co-variates as "clinically-relevant" must be supported by the literature.

RESPONSE: We pre-established a set of co-variates for asthma management behaviors through an a priori consensus of study co-investigators and knowledge-users, which included primary care physicians, respirologists, patient representatives, health system representatives, asthma educators. Our criteria included factors that we believed were practically measurable, clinically-relevant, and plausibly explanatory. For example, although there are no available data on whether after-hours appointments are less likely to be associated with comprehensive asthma care than on-hours appointments, there are ample data demonstrating that in hospitals, quality of care and outcomes are inferior on weekends compared to weekdays, across a number of diseases. This may suggest a similar phenomenon in asthma, and in the outpatient setting. In addition, our primary care co-investigators suggested that this should be included, as their own experience suggested that clinicians might be more inclined to provide best care during regular appointments, and to only manage urgent issues during off-hours appointments (when clinic staffing is also lower). Where possible, covariates were also grounded in existing literature. For example, there is a known association between poor asthma control and prior emergency room or hospitalizations. In one US study, poorly controlled patients had a ten fold higher risk of emergency asthma care than well controlled patients (Guilbert TW, et al., J Asthma. 2011). These data led us to hypothesize that the patients with a prior emergency room visit or hospitalization might have a higher chance of having their asthma control status assessed by their clinician. Similarly, given that patients with an asthma action plan have a lower chance of requiring an emergency room visit, we hypothesized that physicians may be more likely to provide patients with a prior emergency room visit with an asthma action plan, to reduce future risk. The process for co-variate selection has now been better elucidated in the paper (page 8, paragraph 2)

5. Analysis: Please indicate what specifically the interrater reliability measures. I believe that the percent agreement (the concept of "agreement among raters") is fairly simple. Did the authors consider a more complex method (such as kappa statistic) to measure interrater reliability? Please comment the use of percent agreement considering its inability to account for chance agreement.

RESPONSE: As the reviewer correctly points out, kappa is much better at measuring reliability than percent agreement. We initially used a Fleiss' kappa to determine the agreement amongst the 4 reviewers. However, there were several variables which we measured agreement on for which there was perfect agreement. Therefore, there was no variability and the kappa statistic was unable to be computed. Thus, for consistency, we elected to report percent agreement across variables.

6. Multivariable logistic regression was used to identify predictors of each outcome. However, univariate analysis is also calculated but it is not mentioned in this section. Please cite it. Moreover, the odds ratio were also presented in the tables, but not mentioned in this section.

RESPONSE: We have added the requested information to the "Analysis" section (Page 8, paragraph 3). We have also adjusted the results table to include the odds ratios and 95% confidence intervals (see Tables 3 and 4).

7. In order to interpret results of the multivariable analysis the assessment of the model goodness-of-fit is essential. However, this information is not in the manuscript. Also, it is not clear what variable selection procedure was used (FORWARD, BACKWARD, and STEPWISE). Please present this information and if statistic revealed good fitting in the final models.

RESPONSE: We thank the reviewer for this inquiry. While the Hosmer-Lemeshow goodness-of-fit test is commonly used to assess the goodness of fit of logistic regression models; as outlined by Harrell (Regression modeling Strategies CH 10.5 page 231), there can be challenges with this method depending on the "choice of how the predictions are grouped." Therefore, we performed the Hosmer-Lemeshow goodness-of-fit test using a range of groupings from 5-14 and found the model fits were adequate (all having p-values > 0.05). Additionally, we used bootstrap sampling to assess the accuracy of the model. This method assesses how well our model would perform on a "new sample" of data selected from the same population. In the first model there was some minor overfitting, as the optimism for the Somers' Dxy was 0.017 and the slope shrinkage factor was 0.96. Similarly, in the second model there was some minor overfitting, as the optimism for the Somers' Dxy was 0.0257 and the slope shrinkage factor was 0.95. With regard to model selection, we did not perform model selection. As outlined in Harrell (Regression modeling Strategies CH 4.3 pages 56-60) model selection techniques may be problematic for a variety of reasons including yielding standard errors of regression coefficients that are biased low, thus leading to falsely narrow confidence intervals. It can also yield p-values that are too small and can lead to overfitting of regression coefficients. We have this added information about the goodness of fit test and model validation to the results section in the manuscript (Page 9, paragraph 2).

8. The authors performed the multivariate logistic analysis in the 4199 eligible visits, however, it is unclear if they used only data from the first (baseline) visit. If not, a sensitivity analysis using only the data from the 1st visit should be considered and discussed to reduce bias.

RESPONSE: As the reviewer has pointed out, there were some patients who were seen multiple times over the time period. Although a mixed model was attempted, there were not enough subjects with repeated measurements, thereby leading to a lack of convergence of the model. Ideally, it would be good to run a sensitivity analysis using only the baseline visit. However, in the first analysis (Asthma Control Assessment), there were only 46 subjects at baseline that had a positive outcome (had asthma control assessed) and in the second analysis (Medication Initiation or Escalation), there were only 39 subjects at baseline that had a positive outcome (had a medication initiated or escalated). This small number of outcomes would limit the predictor analysis in each of these models to only four variables (and even less if we consider that some of our categorical predictors had > 2 categories). Including all the identified variables would leave the models markedly underpowered, with possibly very wide confidence intervals. In addition, there were visit exclusions applied which further reduced the risk of bias. For our primary outcome (Asthma Control Assessment), visits occurring within 1 month after a provider assessed a patient's control (a standard look back period for symptom-based control assessment) were excluded from the analysis. With respect to our secondary outcome (Medication Initiation or Escalation), visits occurring within 3 after a patient had a controller medication initiation or escalation were excluded (a standard period where further medication changes are discouraged, to allow for the prior medication adjustment to take effect). For clarity, these exclusions

are now outlined in the analysis (Page 8, paragraph 3) (previously these were exclusively in table footnotes). However, we have now added our inability to account for repeated measures as a study limitation (Page 15, paragraph 1).

9. Importantly, a subgroup analysis must be performed considering the different practice sites to address any clustering effect.

RESPONSE: We concur with the reviewer that accounting for clustering is important. However, this is typically done when one is not interested in the variable itself, but needs to account for correlation arising from clustering. For example, when looking at multiple sites and comparing treatments between two groups at the multiple sites, we are interested in the treatment effect and not the site effect, which is not explicitly included in the model. We do recognize the clustering effect by site, but this is accounted for in a proper model (i.e. a mixed model with a random effect for site). However, in our analysis we were explicitly interested in site differences and therefore included it as a covariate in the model itself. The standard error of the site variable will account for the variability between sites.

10. In pages 9 and 10, when authors mention "significant predictors", p-values must be cited. Also, the expression " was less/more likely" must be used citing a measure of probability such as odds ratio, rather than absolute or relative frequencies as the authors did. Please correct this.

RESPONSE: We have added p-values as requested (Page 10, paragraph 4, Page 11, paragraph 2). We have also added the odds ratio where requested (Page 11, paragraph 2).

11. Results presented in Table 3 and 4 must be improved. Presenting both columns ("Controller not initiated or escalated" and "Controller initiated or escalated") is redundant, and other information can be added, such as indicating the reference category for each variable used in the logistic model, and ultimately, presenting adjusted odds ratios and their respective 95% Confidence Intervals.

RESPONSE: We thank the reviewer for this guidance. We have made the requested adjustments to Tables 3 and 4, adding a new column with the odds ratios and 95% confidence intervals. We opted to keep both prior columns (control assessed/not assessed in Table 3 and controller added/not added in Table 4), as the percentages are calculated across each row, and we believed it might be confusing to readers to only present one column with percentages.

12. The study of the authors (Sá-Sousa et al. Rev Port Pneu 2014) reported that most patients with non-controlled asthma (88%) perceived their disease as controlled, l, which may hinder them from seeking better asthma control. Please discuss how patient's perception of the symptoms may have influenced the fact that physician did not assess asthma control?

RESPONSE: We concur with the reviewer that patient perception of their own control is likely a determinant of whether their control is formally assessed by their provider. In many cases, as a result of patients habituating to poor control and failing to perceive their poor control a problem, they are less likely to report this as a concern to their provider, and as a result, less likely to have this addressed in their care. Additionally, when assessing control, many providers use a generic approach ("How is your asthma") instead of the five guideline-recommended symptom-based control questions. If a patient incorrectly assumes that his/her asthma control is acceptable, the resulting under-reporting constitutes a missed opportunity for identification of poor control. We have added this to the discussion (Page 12, paragraph 2).

Reviewer: 5
I have reviewed the manuscript ID bmjopen-2018-022506 entitled "Large Care Gaps in Primary Care

Management of Asthma: A Longitudinal Electronic Practice Audit" by Ms Price and colleagues. I reviewed the manuscript focusing on the choice of the statistical methods and analyses. I find the methods adequate.

With regards to the tables and estimates, I have no comments for table 1. The summary measures and p-value estimates in tables 2, 3 and 4 are well presented. There aren't any obvious records/numbers that may suggest out of range errors.

VERSION 2 – REVIEW

REVIEWER	Eduardo Calvo Corbella Centro de Salud Universitario de Pozuelo .Facultad de Medicina.Universidad Autónoma de Madrid .Spain.
REVIEW RETURNED	30-Aug-2018

GENERAL COMMENTS	The autors have modify the requested amendments.

REVIEWER	Rita Amaral Faculdade de Medicina da Universidade do Porto, Porto, Portugal
REVIEW RETURNED	20-Aug-2018

GENERAL COMMENTS	This comprehensive revision is responsive to reviewer comments on the initial submission and is substantially improved. I have no further comments or concerns.